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Title	Risk of loss of decisional capacity for Medical Assistance in Dying (MAiD) and the importance of the Palliative Performance Scale: a retrospective database review
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Reviewer 1	Ellen Wiebe
Institution	UBC, Family Practice, Vancouver, BC
General comments (author response in bold)	[1] p7,l49: that sentence is too long and unclear. **The sentence has been revised for clarity (p.8).** [2] p8,l49: There are results in the Interpretations section. These should be moved to results and only interpretation left there. **We agree with the reviewer. On p.8 we introduce the following statistic in the interpretation section, which was not in the results section: *"Specifically, of the 68 patients in Group 2 only 35 (51%) were identified by the assessor at the time of initial assessment as clearly requiring shortening of their 10-day wait period."* We have removed this sentence from the interpretation section.** [3] p13,l27: another long sentence that should be broken up. **The sentence has been revised for clarity (p9).** [4] References 14 and 21 are duplicates. **Thank you. We have removed the duplicate reference.**
Reviewer 2	Jackson Wu
Institution	Tom Baker Cancer Centre, Oncology, Calgary, Alta.
General comments (author response in bold)	Comments to the Author The authors may wish to address some issues to enhance the clarity of the materials in context: [1] p.4 line 9 "MAID database" should be further elaborated with respect to database construct (e.g. whether constructed for resource management +/- funding purposes), data management (real time, dedicated admin. coordinators of work flow vs. retrospective quality assurance), and data sources through which the final outcomes are ascertained (hospital chart, EMR, linkages). **Thank you for your comment. Within the Methods section, we have added a subheading "Data Sources" which includes expanded information on database management, the type of data collected, data sources and how the data is verified for accuracy. Our database is not linked to the hospital electronic patient record (EPR), rather we obtained REB approval to extract data on variables of interest from the EPR as part of the study.** [2] p.4 line 20 "Data collected included…" – please clarify potentially relevant prognosticators (e.g. labs, symptom distress) for short survival that are excluded in the proposed multivariable analysis. Why did the study team choose those particular independent variables while others are not included? The outcome variable should specify composite-type outcome (as a single outcome variable in a multivariable regression model), to be distinguished from multiple outcome variables in a single regression model as one would expect in "multivariate" modeling. It would be more appropriate to refer the study model as multivariable instead of a multivariate regression analysis.

	We thank the reviewer for his comment. We agree that there are additional independent variables that could possibly aid in prognostication and in predicting loss of decisional capacity for MAiD. Specifically, certain laboratory values such as albumin, or symptom distress scores such as the Edmonton Symptom Assessment System (ESAS) have been demonstrated in the literature as useful prognostic indicators in certain subsets of patients. Unfortunately, data for these variables was not available in a significant number of individuals given the retrospective nature of our study. We agree that there could be value in collecting this data prospectively, and future MAiD research could investigate the impact of these variables on our outcome. **We have changed "multivariate" to "multivariable" throughout the revised manuscript. We have maintained "bivariate".** [3] p.4 Methods should provide a statement of pre-specified hypothesis (pre-specified model) and specific objectives. **We have tried to make clear that descriptive statistics are used to compare patients for which a) reflection periods were not reduced vs, b) reflection periods were reduced, the patient lost capacity, or died. Logistic regression was used to estimate the bivariate/multivariable impact of demographic/clinical features on our outcome (i.e. patients who received MAiD without shortening of 10d reflection-period; vs. patients who had their 10d reflection-period reduced, lost capacity, or died). A ROC analysis is performed to visualize how sensitivity/specificity vary as a function of PPS cut-point. Other measures of diagnostic accuracy are reported, including PPV, NPV, and distance from optimal sensitivity/specificity.** [4] p.4 Statistical analysis: numerous hypothesis tests are used in bivariate analysis (table 1), the purpose of which is unjustified given absence of pre-specified hypothesis or hypotheses. It is unclear how P-values are informative in a retrospective case-control series as they do not inform variable selection (cf. Sun, Shook and Kay, J Clin Epidemiol. 1996;49(8):907-916). Omitting the P-values in Table 1 does not change the content and relevance of observations summarized in Table 1. **We have removed reference to p-values and hypothesis testing throughout the manuscript: i.e. from the abstract and results section, and also from the tables. The following sentence has been deleted from the methods section.** ***i.e. we have removed: "Fisher's exact test was used to assess the significance of association between pairs of categorical variables. Statistical significance was set at $p \leq 0.05$."*** [5] p.4 Statistical analysis: variable "prior palliative care contact" (Table 1) has too few observations of absence (of prior palliative care contact) which leads to large standard error (Table 2 95% CI) and should be removed; associated P-value of 0.046 is unreliable and misleading. **We thank for reviewer for his comment. We agree that there is limited statistical information in the sample and that this issue is magnified when investigating the association between the variable "Prior Palliative Care Contact" and our outcome. Therefore, we have removed the variable from the Multivariable model, and included a revised table within the manuscript:** **Table 2: Bivariate and Multivariable Logistic Regression Analysis of potential risk**

factors for loss of decisional capacity, death or shortening of 10-day reflection period for MAiD

	Bivariate Logistic Regression	Multivariable Logistic Regression
Variable	Odds Ratio *(95% CI)*	Odds Ratio *(95% CI)*
PPS (Per 10-unit decrease)	4.49 *(2.91, 7.55)*	4.63 *(2.87, 8.23)*
Age (Continuous)	1.02 *(0.997, 1.05)*	0.99 *(0.96, 1.03)*
Sex (Female)	1.34 *(0.69, 2.65)*	1.70 *(0.66, 4.52)*
Location signed written request (Inpatient)	6.88 *(2.89, 18.46)*	1.99 *(0.65, 6.41)*
Diagnosis (Cancer)	0.79 *(0.36, 1.71)*	2.19 (0.71, 7.14)

[6] p.4 Statistical analysis: please clarify any important correlation between independent variables, esp. PPS and location signed (inpatient), that might lead to variance inflation.
A matrix of spearman correlation coefficients, estimating the strength of monotonic dependence between pairs of covariates included in our design matrix is given below. In absolute value, the strongest correlation coefficient is approximately 0.36. We agree with the reviewer that variance inflation can at times be an issue in regression modelling. That said, we do not include the estimated correlation matrix in the manuscript. Nor do we discuss the issue of variance inflation in the paper (mainly because of space limitations, but also because no overly strong correlations are noted below). We acknowledge that if the design matrix was indeed rank deficient (or closely ill-conditioned), that parameter estimability/stability and/or variance inflation would be more of an issue. This is not the case in our study/model.

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> cor(cor_mat, method="spearman")
                   PPS_FormA         Age       Gender Location_Request    Diagnosis PallCare_Contact
PPS_FormA         1.00000000 -0.27004831 -0.019471727      0.348066835  0.238143267      -0.09196040
Age              -0.27004831  1.00000000 -0.176288600     -0.224791265 -0.366214627       0.08776202
Gender           -0.01947173 -0.17628860  1.000000000      0.005949034  0.003464911      -0.14668787
Location_Request  0.34806684 -0.22479127  0.005949034      1.000000000  0.210358852      -0.15078572
Diagnosis         0.23814327 -0.36621463  0.003464911      0.210358852  1.000000000       0.36088247
PallCare_Contact -0.09196040  0.08776202 -0.146687869     -0.150785724  0.360882473       1.00000000
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[7] Loaded phrasing: please reconsider appropriateness of using “wait period”, “wait times” throughout the manuscript to reference the “10 clear days” between request and provision as stipulated by legislation. Since the 10-day period, which could be appreciated as a reflection period, is by legal design a safeguard, the connotation of a “wait time” passes judgement unnecessarily, and perhaps unintentionally, on the period as being a negative effect on care, which is not itself the subject of this investigation. Alternatively, the intent and potential value of the period as a safeguard should be articulated more clearly in the Introduction section, to balance the commonly negative connotation of “wait time”.
We agree with the Reviewer that use of the term “wait time” to refer to the “10 clear days” as stated in the Canadian MAiD legislation is loaded wording on our part, and by its nature infers a negative connotation. In order to remove any perceived bias or negative implication, we have changed any reference to the “10 clear days” in the manuscript to be stated as a “reflection period”.

[8] Patient preference for undergoing provision within the 10-day period (or not) is not disclosed in the study. Clarification is required concerning whether all of the patients were indeed ready and wanting provision within the 10-day period. If there were patients wishing for

	provision after the 10-day period (which would nullify the concept of "wait time"), the study question may itself be conditional on patient factors not yet addressed in this study. Appraisal of the implication of results illustrated in Figure 2 cannot be offered until the a priori patient preference is clarified. **We agree that patient preference around timing of MAiD is important. Many patients did specifically request early provision, ie during the reflection period, but did not receive early provision as there was no indication capacity was in jeopardy. Others wanted provision in advance of the reflection period *and* had clinical findings consistent with high risk of losing capacity and hence received MAiD prior to completing the reflection period. For the group of patients felt to be at high risk of losing capacity discussions were routinely held outlining the option of accelerated provision as well as the option of ongoing care with plans for alternatives to MAiD should they ultimately lose capacity. No patient who did not clearly express a desire to proceed with MAiD went on to receive MAiD, and all of the patients in the subgroup 'lost capacity or died' had a date for MAiD booked but ultimately could not proceed based on the changes in their clinical course. This has been clarified in the methods section.**